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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	29

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/634,039	Snider et al
Examiner	**Art Unit**
F. Pierre VanderVegt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Feb 22, 2001*

2a) X This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-9* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) *1-9* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)	18) ☐ Interview Summary (PTO-413) Paper No(s).
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	19) ☐ Notice of Informal Patent Application (PTO-152)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).	20) ☐ Other

DETAILED ACTION

Claims 1-9 are currently pending in this application.

1. In view of the amendment filed February 22, 2001, only the following rejections are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Estrada et al (38 on form PTO-1449) in view of McDermott et al (10) and Hamaleers et al (15), all of record.

It was stated previously: "The Estrada et al reference teaches immunization of subjects via the intestinal mucosa using antigen covalently conjugated to anti-MHC Class II antibodies (see entire document). Estrada et al further teaches that these conjugates effectively induce production of IgA and IgG antibodies in mice (Abstract in particular). Estrada et al also teaches that conjugation was effected via the hetero-bifunctional cross-linker SMPB (page 902, first column in particular). Estrada et al does not teach intranasal administration. McDermott et al teaches that the respiratory tract possesses lymphoid aggregates similar to the Peyer's patches (PP) of the intestinal wall (paragraph bridging pages 57 and 58 in particular) termed BALT and that the lymphoepithelium of BALT resembles that of the PP (last paragraph of page 59 in particular). McDermott et al further teaches that BALT is exposed to inhaled antigens because of its location (last paragraph of page 63 in particular). McDermott et al further teaches that the gut can be viewed as a model for the lung and that studies of oral immunization can provide insight into respiratory tract immunization (page 93, section D in particular). Hamaleers et al teaches that nasal administration of trinitrophenylated (TNP) keyhole limpet hemocyanin (KLH) induced the production of IgA and IgG antibodies to TNP. KLH is commonly used in the art as a carrier for immunogenic haptens, as it is a classical stimulator of helper T cells through classical pathways. Hamaleers et al teaches the administration of the immunogen as liquid drops. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to immunize a subject according to the manner of Hamaleers et al substituting the KLH carrier with an anti-MHC Class II antibody as taught by Estrada et al. One would have been

motivated to make the substitution with a reasonable expectation of success based upon the teachings by McDermott et al that the BALT of the respiratory tract is functionally similar to the PP of the intestines and the teachings of Estrada et al that the antibody conjugates specifically targeted the antigen presenting cells in the intestine. One would have been further motivated by the teachings of McDermott et al that local humoral immunity plays an important role in respiratory tract defense against airborne pathogens."

Applicant's arguments filed February 22, 2001 have been fully considered but they are not persuasive.

Applicant contends that the specification shows evidence of surprising results over the combination of the prior art teachings. Applicant argues that the Estrada reference shows poor and inconsistent results with the oral administration of the conjugates, leading to direct duodenal injection of the conjugates. This statement only lends support to the combination of the reference with the intranasal application by McDermott. As stated previously, the BALT lymphoid aggregates of the respiratory tract are similar to the Peyer's patches of the intestinal wall. Duodenal injection of the conjugates would bypass the degradative forces of the stomach, allowing more intact conjugate to interact with the Peyer's patch lymphoid aggregates. Duodenal injection is difficult and the idea thereof would not be appealing to subjects. Since the lymphoepithelium of BALT resembles that of the Peyer's patches, it would be well appreciated by the artisan that access to BALT by therapeutic substances if far simpler and less invasive than duodenal injection. Applicant points out that the research group of Estrada et al never published any follow-up studies and asserts, without basis, that it is due to non-promising results. This is not found to be relevant because lines of investigative research are abandoned in the real world for a multitude of reasons including, for example, funding issues, change of direction or break-up of a research group. In regard to Applicant's continued reference to Hamaleers (Cell Tiss. Res) and Koornstra, it is pointed out that the references were never submitted with any reply by Applicant, nor were the references ever made of record in an IDS or on a form PTO-892. Therefore the Examiner will continue to not consider these references or comments.

3. Claims 1-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Estrada et al (38 on form PTO-1449) in view of McDermott et al (10), Hamaleers et al (15) and Babington, U.S. Patent 4,228,795 (C on form PTO-892).

It was stated previously: "Estrada et al, McDermott et al and Hamaleers et al have been discussed supra. The combination of references does not teach a disperser for dispersing an aerosol. Hamaleers et al further teaches that a large proportion of aerosolized antigens wind up in the intestines (page 119 in particular). McDermott et al teaches that this is due to swallowing and results in presentation to the immunological apparatus of the intestines (page 48 in particular). The '795 patent teaches a nebulizer which can be used to aerosolize medicants for nasal inhalation (Figure 4 and column 6, line 7 through column 8, line 54 in particular). The '795 patent further teaches that said nebulizer is suitable for use with viscous or sticky substances (column 8, lines 34-37 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the nebulizer taught by the '795 patent to administer the mAb-pathogenic antigen conjugate taught by Estrada et al to the nasal mucosa as taught by Hamaleers et al. One would have been motivated, with a reasonable expectation of success to combine these teachings by the desire to elicit an antigen-specific, rather than generalized, response in the mucosa, which is often the first line of encounter of an immune system with pathogenic organisms and by the teachings of the '795 patent that the nebulizer is usable with sticky substances, which a common property of proteinaceous solutions. Further motivation for using the nebulizer of the '795 patent is provided by the knowledge that some individuals do not tolerate nose drops well."

Applicant has made no further remark regarding the substance of this rejection. Accordingly, the ground stands unaltered in light of Examiner's response in paragraph 2 supra.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2001 365-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
April 26, 2001

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SUPERVISORY PATENT EXAMINER
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